REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. CLAIM STATUS AND AMENDMENTS

Claims 1-26, 30, 32-37, 39 and 40 were pending in this application when last examined.

Claims 30, 32-37, 39 and 40 were examined on the merits and stand rejected.

Claims 1-26 were withdrawn as non-elected subject matter.

Claims 30 and 37 are amended. The basis for "exhibiting an antagonistic activity against HGF" in claim 30 is in the specification, page 26, line 22 to page 27, line 2.

Claims 30 and 37 are further amended for clarity.

No new matter has been added.

II. ENABLEMENT REJECTION

On pages 3-5 of the Office Action, claims 32-37 and 39-40 were rejected under 35 U.S.C. § 112, first paragraph, for failing to meet the enablement requirement.

Applicants respectfully traverse this rejection as applied to the amended claims. In particular, it is noted that claims 30 and 37 are amended to replace the term "represented by" with the term "of". It is further noted that on page 3, the Examiner has interpreted the phrase "represented by SEQ ID NO: 4" to be interpreted broadly to encompass proteins which have a structure "similar" at SEQ ID NO: 2. Without acquiescence, the claims have been amended and therefore this rejection is overcome for reasons which are self-evident.

III. OBVIOUSNESS REJECTIONS

On pages 8-13 of the Office Action, claims 30, 32 and 34-37 and 39 were rejected under 35 U.S.C. § 103(a) as obvious over Folkman et al. (US 6,024,688) in view of Kuba et al. (Cancer Res., 2000), Nakamura (EP 1074264), Nakamura (EP 1074264) and Seki et al. (Biochem. Biophys. Res. Commun., 1990).

Further, on pages 14-16, claims 30 and 40 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Folkman et al. (US Patent 6,024,688) in view of Kuba et al. (Cancer Res. (2000)), Nakamura, T. (EP 1074264), Nakamura, T. (WO 99/55361) and Seki et al.

(Biochem. Biophys. Res. Commun.(1990)) as previously applied to claims 30, 32 and 34-37 and 39, and further in view of Medico et al. (US 6,551,991) and Mooney et al.(US 5,885,829).

Applicants respectfully traverse these rejections as applied to the amended claims.

The Examiner states "it would be *prima facie* obvious to transform various cells with the cDNA encoding the human HGF/NK4(del5) of Nakamura (i.e. the polynucleotide sequence of SEQ ID NO:2 encodes NK4(del5) polypeptide of SEQ ID NO:4) to inhibit angiogenesis, metastasis and proliferation in the *ex vivo* therapy method of Folkman, particularly because, Kuba teaches that like angiostatin, NK4 is a potent angiogenic inhibitor" .

However, the method of amended claim 30 is a method for exhibiting an antagonist activity against HGF, not a method for inhibiting angiogenesis.

Unlike NK4, angiostatin does not exhibit an antagonist activity against HGF, as proved by §1.132 Declaration of Dr. Matsumoto (No. 1) attached hereto [Attachment A]. Therefore, Folkman does not disclose an *ex vivo* therapy method for exhibiting an antagonist activity against HGF.

Accordingly, there is no motivation to transform cells with the cDNA encoding NK4 of Nakamura in the *ex vivo* therapy method of Folkman to exhibit an antagonist activity against HGF.

As a result, the invention of claim 30 is unobvious from the cited references.

Further, as it is clear from amended claim 30, fibrous protein and biodegradable resin are required in addition to cells having the NK4 gene in claim 30. The specific combination of the two features with cells is neither disclosed nor suggested in the Folkman reference. The combination is the gist of the claimed invention of this case as fully stated in the response filed April 2, 2009. Therefore, it is abundantly clear that the claimed invention has unobviousness.

Since the inventions of claims 32-37 and 39-40 comprise all elements of the invention of claim 30, the inventions of claims 32-37 and 39-40 are unobvious from cited references.

In addition, the method of claim 40 exhibits surprising advantageous effect. That is, the method achieves extremely large production of NK4 by using epithelial cells of the oral mucosa.

Specifically, as shown in §1.132 Declaration of Dr. Matsumoto (No. 2) [Attachment B], when DNA encoding NK4 is infected to various types of cells using adeno-associated virus(AAV) vector, NK4 production of epithelial cells of the oral mucosa is 44-times or more than that of pancreatic cancer cells, lung carcinoma cells, or melanoma cells.

This is a surprising advantageous effect that supports the unobviousness of the invention of claim 40.

Thus, for the above noted reasons, these rejections are untenable and should be withdrawn.

IV. OBJECTION OF CLAIM 37

On page 13 of the Office Action, claim 37 was objected to for being a substantial duplicate of claim 30.

Applicants respectfully traverse this rejection as applied to the amended claims.

Claim 30 is drawn to a cell-containing preparation comprising a cell which has a DNA having a base sequence of SEQ ID NO: 2 or a DNA encoding a protein having amino acid sequence of SEQ ID NO: 4. It is noted that the genus of DNA's which encode a protein having an amino acid sequence of SEQ ID NO: 4 is larger than the genus of DNA's having a base sequence of SEQ ID NO: 2 due to code degeneracy. It is further noted that claim 37 is limited to SEQ ID NO: 2. Therefore the scopes of these two claims are different and this rejection is untenable.

V. INDEFINITENESS REJECTION

On pages 13-14 of the Office Action, claims 30, 32-37 and 39-40 were rejected under 35 U.S.C. 112, second paragraph, as indefinite for the noted reasons. Without acquiescence to the correctness of this rejection, claims 30 and 37 are amended to recite "of" instead of "represented by". Thus, this rejection is overcome for reasons which are self-evident.

CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

Takehisa MATSUDA et al.

By: /William R. Schmidt, II/

Digitally signed by /William R. Schmidt, II/
DN: cn=/William R. Schmidt, II/, o=WLP, ou, email=bschmidt@wenderoth.com, c=US
Date: 2009.11.02 16:00:40 -05'00'

William R. Schmidt, II
Registration No. 58,327
Attorney for Applicants

WRS/vah
Washington, D.C. 20006-1021
Telephone (202) 721-8200
Facsimile (202) 721-8250
November 2, 2009